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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,823	12/19/2005	Joergen Hansen	14455.880US01	5908

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EXAMINER	
JOIKE, MICHELE K	
ART UNIT	PAPER NUMBER
1636	

NOTIFICATION DATE	DELIVERY MODE
03/26/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/561,823	HANSEN ET AL.	
	Examiner	Art Unit	
	Michele K. Joike	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,7,8,19 and 21* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,4,7,8,19 and 21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on March 5, 2010 has been entered.

Claims 1, 2, 4, 7, 8, 19 and 21 are pending and examined.

Claim Objections

Claim 21 is objected to because of the following informalities: There is a hyphen between "an" and "enzyme" in line 2 that should not be present. Appropriate correction is required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 4, 7, 8, 19 and 21 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Moehs et al, Day et al, Arend et al and Priefert et al.

Response to Arguments Concerning Claim Rejections – 35 USC § 103 (a)

Applicants' arguments filed March 5, 2010 have been fully considered but they are not persuasive.

Also, the declaration under 37 CFR 1.132 filed March 5, 2010 is insufficient to overcome the rejection of claims 1, 2, 4, 7, 8, 19 and 21 as set forth in the last Office action because: the arguments in the declaration concerning the 35 U.S.C. 103(a) have not been found persuasive as discussed below.

The following grounds of traversal in the 1.132 declaration and Applicants' arguments are presented:

Applicants argue that as taught by the specification, the microorganism with the glycosyltransferase present surprisingly produces higher amounts of the aglycon than a microorganism without the glycosyltransferase present. The cited references fail to teach this. In Moehs et al, a solanidine glycosyltransferase (SGT) was tested for activity in an in vitro assay. It does not teach whether the yeast could produce the glycosylated form of solasodine in vivo. It also does not teach glycosylation inside the cell. Furthermore, Moehs advises to downregulate SGT expression to reduce the level of the accumulated glucoside, which is opposite of the instant application which teaches increasing the level of the desired glucoside. The purpose of glycosylation in Moehs is to render the aglycon less toxic so deglycosylation is contra-indicated as it would inhibit yeast growth. Therefore, Moehs teaches away from the present development.

Neither Day nor Preifert remedy the deficiencies of Moehs. They do not teach introduction of genes into yeast for production of a glycosyltransferese for the production of a glycosylated aglycon.

Arend also does not cure the deficiencies of Moehs. Arend merely teaches transforming E. coli with a gene encoding a glycosyltransferase, but then adding the aglycon to the medium.

None of the references teaches both production of the aglycon vanillin and the glycosylated form of vanillin in the same yeast cell. It is clear that claim 1 specifically claims the dual biosynthesis pathways for both vanillin and the glycosyltransferase within a yeast microorganism yielding production of vanillin and glycosylated vanillin. Applicants also dispute the statement by the Examiner in the previous office action that "there is reason to believe that glycosylating other aglycons will be successful."

Applicants' arguments have not been found persuasive for the following reasons.

Moehs et al teach the introduction of SGT into a yeast cell for the production of a glycosylated aglycon. They also teach adding the aglycon to the media in order to be glycosylated. They do not teach that the cell has a gene encoding a product involved in the biosynthesis pathway leading to the aglycon. However, Priefert et al teach the production of vanillin, wherein the cell comprises a gene encoding a product involved in the biosynthesis pathway leading to the aglycon. For example, Pseudomonas strain HR199 has genes leading to the production of vanillin. (This is taught by Priefert et al, however, reference Overhage et al was provided in the advisory action as further

evidence.) Therefore, one of skill in the art would know that vanillin biosynthetic genes could be used in a microorganism, as opposed to merely supplementing the media with the aglycon. Combined with Day et al and Arend et al, the references teach the claimed invention. Furthermore, as argued previously by the Examiner, claim 1 does not claim the vanillin biosynthetic pathway, but a method for producing vanillin, wherein a gene involved in the biosynthesis is present. In response to the statement disputing that "there is reason to believe that glycosylating other aglycons will be successful", the Examiner still believes there is a reasonable expectation of success for glycosylating aglycons, as Arend et al teaches the glycosylation of vanillin, and other aglycons.

Moehs does teach higher amounts of glycosylated solanidine in vitro, and this proves that the presence of a glycosyltransferase can increase production of a glycosylated aglycon. Since Moehs and Arend teach that glycosyltransferases can be produced in vivo, and Prieffert teaches that genes involved in vanillin boiosynthesis can be present in the cell, there is no reason to believe that glycosylation of vanillin cannot occur in vivo.

The Examiner disagrees Moehs teaches away. Moehs does not advise to downregulate SGT expression to reduce the level of the accumulated glucoside. It merely states that SGT regulation is being investigated and that down-regulation occurs by the use of anti-sense RNA. It further states that analysis of SGT down-regulation will help further charaterization of the enzyme. Affecting activity of an enzyme is a common way to characterize an enzyme. It does not mean that Moehs is advocating downregulating activity of the enzyme. Also deglycosylation is not contra-indicated. As

Applicants have pointed out, glycosylation is perofrmed in vitro. It is unlikey the glycosylated aglycon would be transported into the cell to be de-glycosylated. Therefore, de-glycosylation will not affect cell growth.

The Examiner agrees that none of the references individually teach the dual biosynthesis of a glycosyltransferase and an algycon. However, as discussed in the prior office actions, combined, the references teach the method in claim 1.

Lastly, as discussed above, the higher yields seen by Applicants is not unexpected or surprising, as Moehs teaches increased production with the presence of a glycosyltransferase.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 10:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571)272-0951. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K. Joike/
Primary Examiner, Art Unit 1636

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